



Emin, A., Rogers, C. A., & Banner, N. R. (2016). Quality of life of advanced chronic heart failure: medical care, mechanical circulatory support and transplantation. *European Journal of Cardio-Thoracic Surgery*, 50(2), 269-273. <https://doi.org/10.1093/ejcts/ezw054>

Publisher's PDF, also known as Version of record

Link to published version (if available):
[10.1093/ejcts/ezw054](https://doi.org/10.1093/ejcts/ezw054)

[Link to publication record in Explore Bristol Research](#)
PDF-document

This is the author accepted manuscript (AAM). The final published version (version of record) is available online via Oxford Academic at <https://academic.oup.com/ejcts/article/50/2/269/2237763/Quality-of-life-of-advanced-chronic-heart-failure> . Please refer to any applicable terms of use of the publisher.

University of Bristol - Explore Bristol Research

General rights

This document is made available in accordance with publisher policies. Please cite only the published version using the reference above. Full terms of use are available:
<http://www.bristol.ac.uk/red/research-policy/pure/user-guides/ebr-terms/>

Akan Emin^a, Chris A. Rogers^{a,b} and Nicholas R. Banner^{c,*}, On behalf of the Steering Group,
UK Cardiothoracic Transplant Audit

^a Clinical Effectiveness Unit, The Royal College of Surgeons of England, London, UK

^b Clinical Trials and Evaluation Unit, School of Clinical Sciences, University of Bristol, Bristol, UK

^c Royal Brompton and Harefield NHS Foundation Trust, Harefield Hospital, Harefield, Middlesex, UK

* Corresponding author. Transplant Medicine and Circulatory Support, Royal Brompton and Harefield NHS Foundation Trust, Harefield Hospital, Hill End Rd, Middlesex UB9 6JH, UK. Tel: +44(0)-1895-823737; e-mail: n.banner@rbht.nhs.uk (N.R. Banner).

Received 22 March 2015; received in revised form 13 January 2016; accepted 25 January 2016

Abstract

OBJECTIVES: Advanced chronic heart failure (ACHF) is progressive with poor prognosis and quality of life (QoL). Heart transplantation (HTx) is an effective treatment for ACHF, but is limited by scarcity of donor hearts. Left ventricular assist device (LVAD) support is a useful bridging therapy, and short- and medium-term outcomes have improved. We investigated QoL in patients assessed for HTx, awaiting HTx and after HTx.

METHODS: We carried out a cross-sectional survey across four groups: Group 1—patients assessed for HTx, Group 2—patients listed for HTx on medical therapy, Group 3—patients supported with LVAD and Group 4—patients after HTx. Two questionnaires, the Kansas City Cardiomyopathy Questionnaire (KCCQ) and the EuroQol dimensions (EQ-5D), were administered in all adult HTx centres in the UK. Scores calculated for the KCCQ and EQ-5D were compared.

RESULTS: Three hundred and eighty-six patients completed questionnaires: 194 in Group 1, 28 in Group 2, 82 in Group 3 and 82 in Group

4. Patients after HTx reported the best QoL [KCCQ overall summary score: mean 73.0 (SD 27.2)]; patients with LVAD reported better QoL than those being assessed for HTx and those listed for HTx on medical therapy [overall summary score; LVAD: 52.6 (22.0), Listed on medical therapy: 33.3 (21.1), Assessment: 35.5 (21.5)]. Similarly, EQ-5D scores were highest in patients after HTx [HTx: mean 0.74 (0.27); LVAD: 0.58 (0.26), Listed on medical therapy: 0.44 (0.27), Assessment: 0.50 (SD 0.30)].

CONCLUSIONS: Patients supported with LVAD had a significantly better QoL than those awaiting HTx without LVAD support, although HTx patients reported the best QoL.

INTRODUCTION

Heart failure (HF) is a progressive condition and advanced chronic HF (ACHF) is associated with a poor prognosis and poor quality of life (QoL) [1, 2]. Heart transplantation (HTx) is an effective treatment for selected patients, but it is limited by the scarcity of suitable donor hearts, resulting in increasing waiting times before transplantation [3].

Left ventricular assist devices (LVADs) have been used as an adjunct to HTx, bridging patients to transplant when organs have not been available and this has become more frequent due to the scarcity of donor hearts [4]. Currently, in the UK, LVAD support is restricted to bridging patients to transplantation because of concern regarding the cost and cost-effectiveness of such therapies [5]. QoL has been shown to improve after LVAD implantation and after HTx [6–11]. However, a direct comparison of transplant candidates receiving medical therapy, LVAD support and after HTx has not been undertaken. Here, we report the results of a multicentre cohort study of QoL in ACHF patients.

METHODS

The UK Cardiothoracic Transplant Audit (UKCTA) is an ongoing prospective cohort study involving all UK HTx centres, which has collected data on all patients listed for HTx and patients who received allografts since April 1995. Data on LVAD activity and outcome (demographic data and follow-up data for survival, explant and transplant) have been collected since 2002. In 2006, a more comprehensive database of VAD activity and outcome was established for the purposes of audit and research. This study was conducted by the UKCTA with participation of all UK HTx centres as an extension of the national audit agreed between commissioners and centres. Additional QoL data were collected over an 18-month period.

Participants and recruitment

Questionnaires were distributed to patients within four defined populations when they attended hospital over an 18-month period between January 2011 and August 2012.

We included all adult patients assessed for HTx (Group 1: *Assessment*); all patients listed for HTx without an LVAD *in situ* (Group 2: *Listed for HTx on medical therapy*); all patients with an LVAD *in situ* (Group 3: *LVAD*) and all adult patients (aged 16 years or more) who underwent HTx between January 2009 and December 2010 (Group 4: *post-HTx*).

All NHS adult HTx centres participated in the study. These are the Royal Brompton and Harefield Trust, Harefield Hospital (London), Queen Elizabeth Hospital (Birmingham), Papworth Hospital (Cambridge), Freeman Hospital (Newcastle), Wythenshawe Hospital (Manchester) and Golden Jubilee Hospital (Glasgow).

Completed questionnaires were returned to the Royal College of Surgeons of England (RCS) where they were entered into a purpose-

designed database. The questionnaires included a minimal set of identifiers that allowed the data to be linked to the UKCTA transplant and VAD databases to determine the patient group. The UKCTA transplant database includes all patients listed for HTx and all patients who have received HTx, whereas the VAD database includes all NHS patients who have had LVAD support. Questionnaires which could not be successfully linked to either database were checked with the centre to confirm they were returned by a patient being assessed for HTx. The audit does not routinely collect data on patients being assessed for HTx.

Quality-of-life instruments

The validated QoL instruments used included one disease-specific measure: the Kansas City Cardiomyopathy Questionnaire (KCCQ) and one generic measure: the EuroQol 5 dimensions (EQ-5D) [12]. The KCCQ is a 23-item questionnaire developed to describe QoL in patients with HF. It quantifies physical limitation; symptom stability, frequency and burden; QoL; social interference and self-efficacy. These scores are then used to derive a total symptom score, overall summary score and clinical summary score [12]. The KCCQ was chosen in preference to other disease-specific measures due to its excellent sensitivity to clinical change in patients with HF [12, 13]. A 5-point change in the overall summary score longitudinally is considered to reflect a clinically significant change in HF status [12]. For all scores, higher values indicate a better QoL.

The EQ-5D defines health in five dimensions: morbidity, self-care, usual activities, pain or discomfort, anxiety or depression, which are combined to give a state score [14]. The EQ-5D has a broader user base than the KCCQ and is well recognized as a generic measure which is short and easy to use for both the administrator and the patient. Again, higher state scores represent a better QoL. A value of 1 indicates full health and a value of less than zero indicates a QoL worse than death. The EQ-5D also returns scores from a visual analogue scale, a self-reported percentage where 100% represents full health.

Statistical methods

Continuous variables are summarized using a mean and standard deviation or median and interquartile range if the distribution is skewed, and categorical variables are reported as a number and percentage. Patient characteristics are compared using the Kruskal–Wallis test (continuous variables with a skewed distribution) and χ^2 test (category variables with expected frequencies greater than 5). Questionnaire scores are compared using analysis of variance (continuous variables with an approximate normal distribution). Statistical analyses were carried out using Stata version 11.2.

Ethics

Ethical approval was not required for this study as confirmed by the UK National Ethics Service.

RESULTS

Questionnaires completed

Questionnaires were received from the six HTx centres during the study period. In total, 389 patients returned a questionnaire; 3 were excluded from the analysis due to the lack of sufficient identifiers to facilitate data linkage, leaving 386 questionnaires. Case ascertainment was not complete; centre coordinators administered questionnaires when the patient attended hospital and patient participation was voluntary. In total, 286 patients were listed for HTx within the study period; questionnaires were returned from 194 patients assessed for HTx (not all of whom will have subsequently been listed for HTx) and 110 patients on the national waiting list (28 on medical therapy and 82 with an LVAD *in situ*). Overall, 180 HTx were carried out between January 2009 and December 2010 and questionnaires were returned by 82 patients post-HTx. The median time from HTx to questionnaire completion was 332 days [interquartile range (IQR) 168–623 days].

Patient demographics

Patient demographics of the four patient groups are summarized in Table 1. The median age was 50.1 years (IQR 41.1–57.8, $n = 385$). Hypertension was more prevalent among post-HTx recipients and previous stroke occurred more frequently in patients with an LVAD. Employment status differed significantly across the groups ($P = 0.005$). Proportionally more patients were in paid employment at assessment (34.8%) and after HTx (34.7%) than at other times (16% if listed on medical therapy and 20% with LVAD support).

Kansas City Cardiomyopathy Questionnaire scores

The 10 KCCQ summary scores are given in Table 2 and Fig. 1. Both patients being assessed for HTx and those listed on medical therapy consistently reported worse mean scores than those with LVAD support. The post-HTx group reported the best mean QoL scores in most modalities (exceptions being symptom stability and self-efficacy scores). The symptom stability scores were best in the LVAD group; mean 60.9 in the patients with LVAD compared with 54.7 in the post-HTx group. Patients with LVAD reported similar self-efficacy mean scores to the post-HTx group.

Table 1: Self-reported patient demography

Variable	(N)	(N)	(N = 28)	(N)	(N)	p
Age in	5	5	47.1	4	5	0
Comorbidi						
Hypertensi	5	1	5 (23.8)	7	2	<
Stroke	2	8	1 (4.6)	1	6	0
Peripheral	5	3	3 (13.6)	1	1	0
Lung	2	1	2 (8.7)	6	5	0
Diabetes	4	2	1 (4.6)	1	1	0
Kidney	2	1	1 (4.6)	5	5	0
Anxiety or	8	3	9 (37.5)	2	2	0
Arthritis	3	2	2 (9.5)	9	7	0
	9	1				0

LVAD: left ventricular assist device; HTx: heart transplantation; IQR: interquartile range.

*Kruskal–Wallis test.

**Chi-squared test.

Table 2: KCCQ and EQ-5D scores: higher scores imply better performance within domains

QoL	Ass	Listed on	LV	Post-	p
domain	ess	medical	AD	st-	-
scores	me	therapy (N =	(N	HT	v
Score	nt	28)	=	x	a
	(N		82	(N	l
	=)	=	u
	19	33.9 (23.8)		82	e
	4)	79.5 (18.7))	*
KCCQ		43.5 (22.5)	60		
domains		47.9 (20.7)	.9		
Sympto	47.	45.7 (20.6)	(2	54	
m	8	34.7 (25.8)	1.	.7	
stability	(29	40.2 (22.0)	7)	(2	
Self-	.5)	24.4 (20.4)	93	1.	<
efficacy	74.	27.3 (27.2)	.8	6)	0
Sympto	2	33.3 (21.1)	(1	93	0

Total symptom score and clinical summary score have been grouped together with domains that contribute to the summary score.

KCCQ: Kansas City Cardiomyopathy Questionnaire; EQ-5D: EuroQol dimensions; QoL: quality of life; LVAD: left ventricular assist device; HTx: heart transplantation; IQR: interquartile range.

*Analysis of variance.

EuroQol 5 dimension scores

EQ-5D index scores are given in Table 2 and Fig. 1. Patients in the LVAD group reported better EQ-5D index scores than medically treated ACHF patients and assessed patients. QoL scores reported by post-HTx patients were better than in all other groups.

DISCUSSION

There are three main findings of our study. First, patients with ACHF receiving medical therapy, those being assessed for HTx and those awaiting HTx without LVAD had very poor QoL. Second, HTx was the most effective surgical treatment in terms of QoL achieved. Third, patients receiving LVAD support for ACHF had a better QoL than those receiving medical treatment despite LVAD patients having been selected, because they were refractory to medical treatment.

Many studies have documented a poor QoL in ACHF, and the impact appears to be related to the stage of the disease [7, 8, 10, 15]. Our study confirmed this finding with similar KCCQ and EQ5D results to those reported by others. Previous studies have demonstrated that both HTx and LVAD support can improve QoL in ACHF [6–8, 10]. A recent study showed improved QoL at 3 months following HTx and LVAD implantation, with an associated increase in levels of habitual physical activity. This was compared with a poorer QoL and lower physical activity in ACHF patients not undergoing HTx or LVAD [16]. Our study is the first to directly compare QoL in ACHF patients receiving medical therapy while awaiting HTx, LVAD support as a bridge to HTx and after HTx.

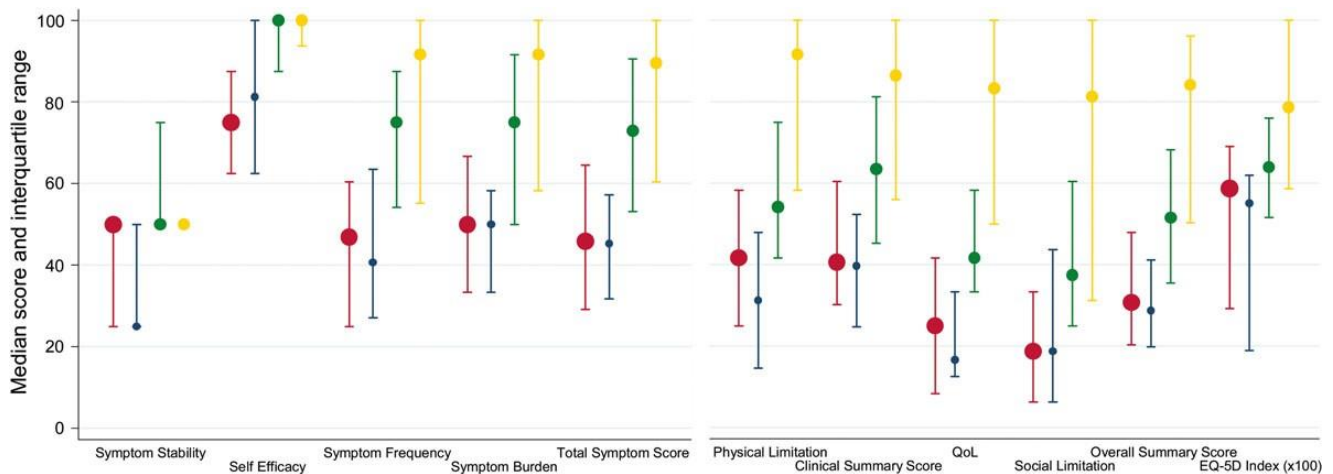


Figure 1: Median scores and interquartile ranges by the study group [assessment group in red ($n = 194$), medical therapy in blue ($n = 28$), LVAD in green ($n = 82$) and post-HTx in yellow ($n = 82$). LVAD: left ventricular assist device; HTx: heart transplantation; EQ-5D: EuroQoL dimensions.

Our study population consisted of ACHF patients within the UK pathway leading to HTx. This pathway involved several stages: referral for HTx assessment and selective listing for HTx, HTx when organs are available or LVAD implantation in the absence of HTx when patients deteriorate. Questionnaire administration time points were chosen to reflect these key stages within the HTx pathway.

Due to advances in LVAD technology, patients with ACHF refractory to medical therapy now have two options. HTx provides best long-term outcome in selected patients, but scarcity of organs means this treatment has a limited availability and the waiting period is long. HTx activity in the UK has decreased in recent years [3], leading to an increasing need for LVAD support [4].

Patients receiving medical treatment for ACHF and being listed for HTx reported the worst QoL in all domains. QoL was best after HTx. Almost all QoL summary scores in patients with HTx were significantly better than all other treatment groups. This may be related to the lower functional capacity of LVAD patients compared with HTx recipients [2–4].

The most important finding in our study was that patients receiving LVAD support report QoL scores that are better than medically treated patients despite the fact that patients who were being treated medically were deemed to be ‘too well’ to currently require an LVAD. Patients selected for LVAD were refractory to medical therapy, more unwell and less stable than those on medical therapy. Despite this, LVAD patients reported a significantly better QoL in all domains [10].

Patients with LVAD support report worse scores for specific elements of physical limitation such as showering. This is expected due to driveline protrusion from the skin, which makes showering and washing more difficult for LVAD patients, necessitating special precautions.

Strengths and limitations

This is the first comprehensive national cohort study to compare QoL in ACHF patients who are potentially eligible for HTx. As is common with patient-completed questionnaires, the response rate was incomplete. No data were collected on those who declined to participate, so we are unable to assess whether those who participated are representative of the cohort as a whole. The limited duration of this study mandated a cross-sectional study design. In future, longitudinal studies may be able to directly observe the effect on QoL of patients moving from medical therapy to LVAD support and ultimately HTx.

We used two of the best known questionnaires to detect clinical changes in HF. Patients who have undergone HTx have technically been ‘cured’ of ACHF and this caused some confusion for certain patients when answering questions regarding ‘their’ ACHF. The questionnaires were used to capture snapshots of QoL within patient episodes and were therefore not able to completely reflect the potential instability of QoL in ACHF patients with changing disease states. There are no specific questionnaires developed with good validation for support with a continuous-flow LVAD; any such QoL instrument would collect data related to specific issues such as restricted activities and showering and problems related to driveline and system care.

Data characterizing the study cohort was limited, particularly for the Group 1 patients referred to HTx assessment; these patients are a heterogeneous group; some will go on to be listed for HTx, some will be considered unsuitable for HTx and others may not be ready for listing but will continue to be monitored. This patient group is not included in the national audit currently and the outcome of the assessment process is unknown. Similarly, Group 2 patients who were listed for HTx under optimal medical treatment include patients in a stable condition and patients with a progressive deterioration that may lead them to require an LVAD and/or an urgent HTx.

CONCLUSION

This study has found that LVAD support provided a significantly better QoL for ACHF patients awaiting HTx than continued medical therapy. However, HTx recipients had an even better QoL and HTx remains the gold standard treatment for such patients when suitable donor hearts are available.

ACKNOWLEDGEMENTS

We thank the UKCTA Project and UKCTA Steering group for their assistance in the implementation of this study. We also thank the VAD forum for their approval and each of the six national cardio-pulmonary transplantation centres in the UK for approving the study and implementing the data collection ([Supplementary Material](#)).

Individually, we thank the following HTx and VAD coordinators for their role in supporting this QoL study; Mike Hedger (Harefield Hospital, London), Rachel Hards (Harefield Hospital, London), Paul Lincoln (Papworth Hospital, Cambridge), Neil Wrightson (Freeman Hospital, Newcastle), Julie Clarkson (Freeman Hospital, Newcastle), Nicole Robinson (Freeman Hospital, Newcastle), Sharon Beer (Queen Elizabeth Hospital, Birmingham), Jane Lockhart (Golden Jubilee Hospital, Glasgow) and Jane Nuttall (Wythenshawe Hospital, Manchester).

Funding

The National Specialized Commissioning Team, NHS UK, funded the UKCTA. This work was carried out independently of the funder. The views and opinions expressed herein are those of the authors and do not necessarily reflect those of the National Specialized Commissioning Team, NHS UK or the UK Department of Health.

Conflict of interest: none declared.

REFERENCES

- [1] Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W *et al.* Long-term use of a left ventricular assist device for end-stage heart failure. *N Engl J Med* 2001;345:1435–43.
- [2] Sharples L, Buxton M, Caine N, Cafferty F, Demiris N. Evaluation of the ventricular assist device programme in the UK. *Health Technol Assess* 2006;10:138.
- [3] Thekkudan J, Rogers CA, Thomas HL, van der Meulen JHP, Bonser RS, Banner NR *et al.* Trends in adult heart transplantation: a national survey from the United Kingdom Cardiothoracic Transplant Audit 1995–2007. *Eur J Cardiothorac Surg* 2010;37:80–6.
- [4] Emin A, Rogers CA, Parameshwar J, Macgowan G, Taylor R, Yonan N *et al.* Trends in long-term mechanical circulatory support for advanced heart failure in the UK. *Eur J Heart Fail* 2013;15:1185–93.
- [5] Clarke A, Pulikottil-Jacob R, Connock M, Suri G, Kandala N-B, Maheswaran H *et al.* Cost-effectiveness of left ventricular assist devices (LVADs) for patients with advanced heart failure: analysis of the British NHS bridge to transplant (BTT) program. *Int J Cardiol* 2014;171:338–45.
- [6] Grady KLK, Jalowiec AA, White-Williams CC, Pifarre RR, Kirklin JKL, Bourge RCR *et al.* Predictors of quality of life in patients with advanced heart failure awaiting transplantation. *J Heart Lung Transplant* 1995;14(1 Pt 1): 2–10.
- [7] Grady KL, Jalowiec A, White-Williams C. Quality of life 6 months after heart transplantation compared with indicators of illness severity before transplantation. *Am J Crit Care* 1998;7:106–16.
- [8] Grady KLK. Quality of life in patients with chronic heart failure. *Crit Care Nurs Clin North Am* 1993;5:661–70.
- [9] Hsich EME, Naftel DCD, Myers SLS, Gorodeski EZE, Grady KLK, Schmuhl DD *et al.* Should women receive left ventricular assist device support? Findings from INTERMACS. *Circ Heart Fail* 2012;5:234–40.
- [10] Dew MAM, Kormos RLR, Winowich SS, Harris RCR, Stanford EAE, Carozza LL *et al.* Quality of life outcomes after heart transplantation in individuals bridged to transplant with ventricular assist devices. *J Heart Lung Transplant* 2001;20:1199–212.
- [11] Sharples LD, Dyer M, Cafferty F, Demiris N, Freeman C, Banner NR *et al.* Cost-effectiveness of ventricular assist device use in the United Kingdom: results from the evaluation of ventricular assist device programme in the UK (EVAD-UK). *J Heart Lung Transplant* 2006;25:1336–43.
- [12] Green CP, Porter CB, Bresnahan DR, Spertus JA. Development and evaluation of the Kansas City Cardiomyopathy Questionnaire: a new health status measure for heart failure. *J Am Coll Cardiol* 2000;35: 1245–55.
- [13] Spertus JA. Evolving applications for patient-centered health status measures. *Circulation* 2008;118:2103–10.
- [14] EuroQol Group. EuroQol—a new facility for the measurement of health-related quality of life. *Health Policy* 1990;16:199–208.
- [15] Dew MAM, Kormos RLR, Roth LHL, Armitage JMJ, Pistas JMJ, Harris RCR *et al.* Life quality in the era of bridging to cardiac transplantation. Bridge patients in an outpatient setting. *ASAIO J* 1993;39:145–52.
- [16] Jakovljevic DG, McDiarmid A, Hallsworth K, Seferovic PM, Ninkovic VM, Parry G *et al.* Effect of left ventricular assist device implantation and heart transplantation on habitual physical activity and quality of life. *Am J Cardiol* 2014;114:88–93.